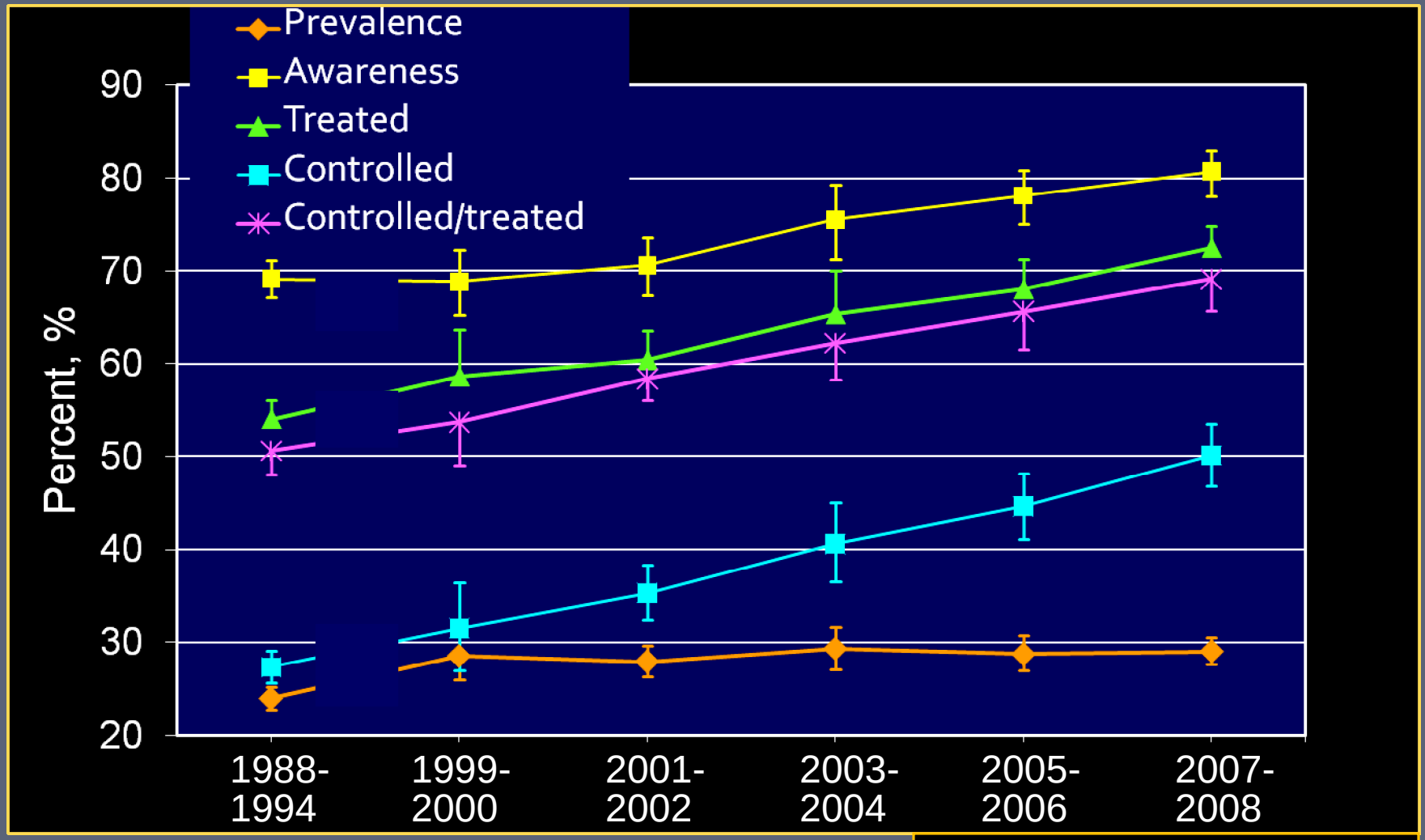
Hypertension Update 2011. Evidence Since JNC 7 that Impacts Patient Care

A case-based approach:

- BP Measurement & Hypertension Dx
- Initial therapy mono-Rx, combo-Rx
- Treatment Resistant Hypertension
- Diabetic Hypertensive
- Elderly and Very Elderly Hypertensive
- Summary

Clinical Epidemiology of Hypertension in the U.S. 1988–2008



JAMA 2010;303:2043ï 2050

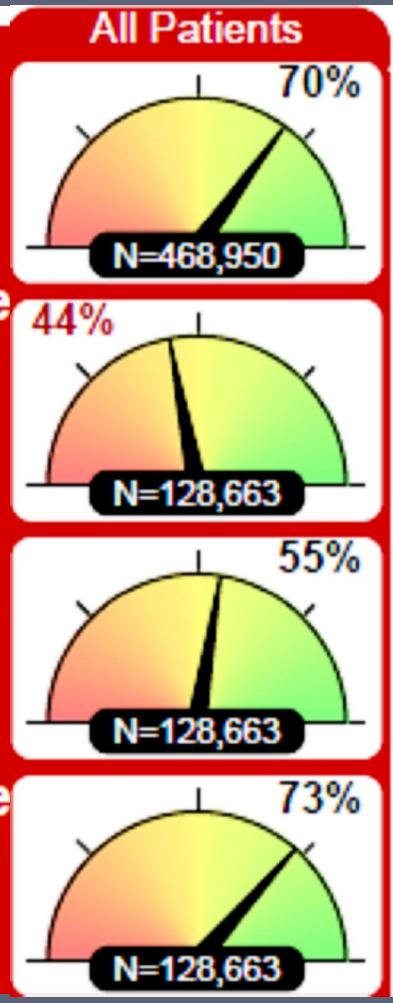
Hypertension Control in O'QUIN 2010

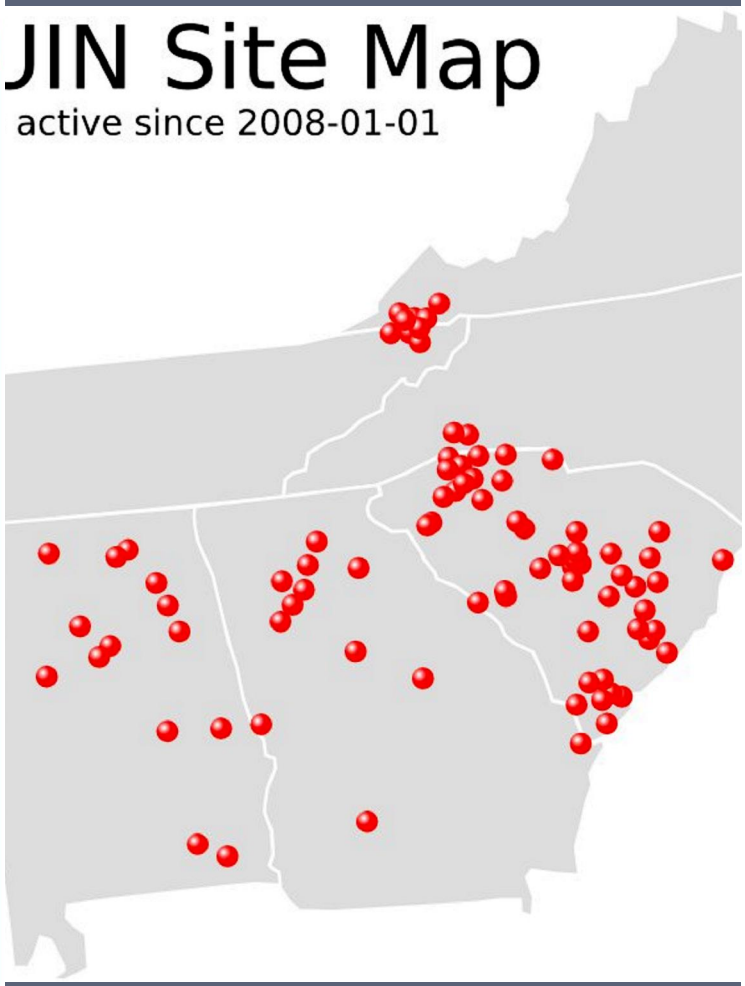
1. NCQA: Controlling High BP.
Goal <140/<90. Pts 18-85 yrs with HTN Dx >6 months before year end.

2. NCQA: Comp. Diabetes Care
Goal <130/<80. Includes all diabetics 18-75 yrs.
Not limited to Dx of HTN.

3. PQRI#3: DM BP Control.
Goal <140/<80. Includes all diabetics 18-75 yrs.
Not limited to Dx of HTN.

4. NCQA: Comp. Diabetes Care
Goal <140/<90. Includes all diabetics 18-75 yrs.
Not limited to Dx of HTN.





Blood Pressure and Diagnosis of Hypertension

History: Mrs. LC is a 52 y/o teacher seen for annual exam. General health good. Walks 20 minutes daily, DASH-like diet, never smoked. Father had HTN and died from CHF age 74. Mother 78 yrs has HTN and T2D, no complications. Older sister has HTN.

At your suggestion last year, LC monitors home BP 2X/d 1 wk/mo. Home BP higher past 6 mo avg 137/86.

Exam: Healthy middle-aged women
BP 136/78 (**avg 5 BpTRU**) HR 74 Wt 148 Ht 66
BMI 23.9 Abd girth: 33" Otherwise unremarkable

Blood Pressure and Diagnosis of Hypertension

Lab: FBS 98 K^+ 4.3 Creat 1.0 (eGFR 62)

Chol 194 TG 127 HDL 51 LDL 118

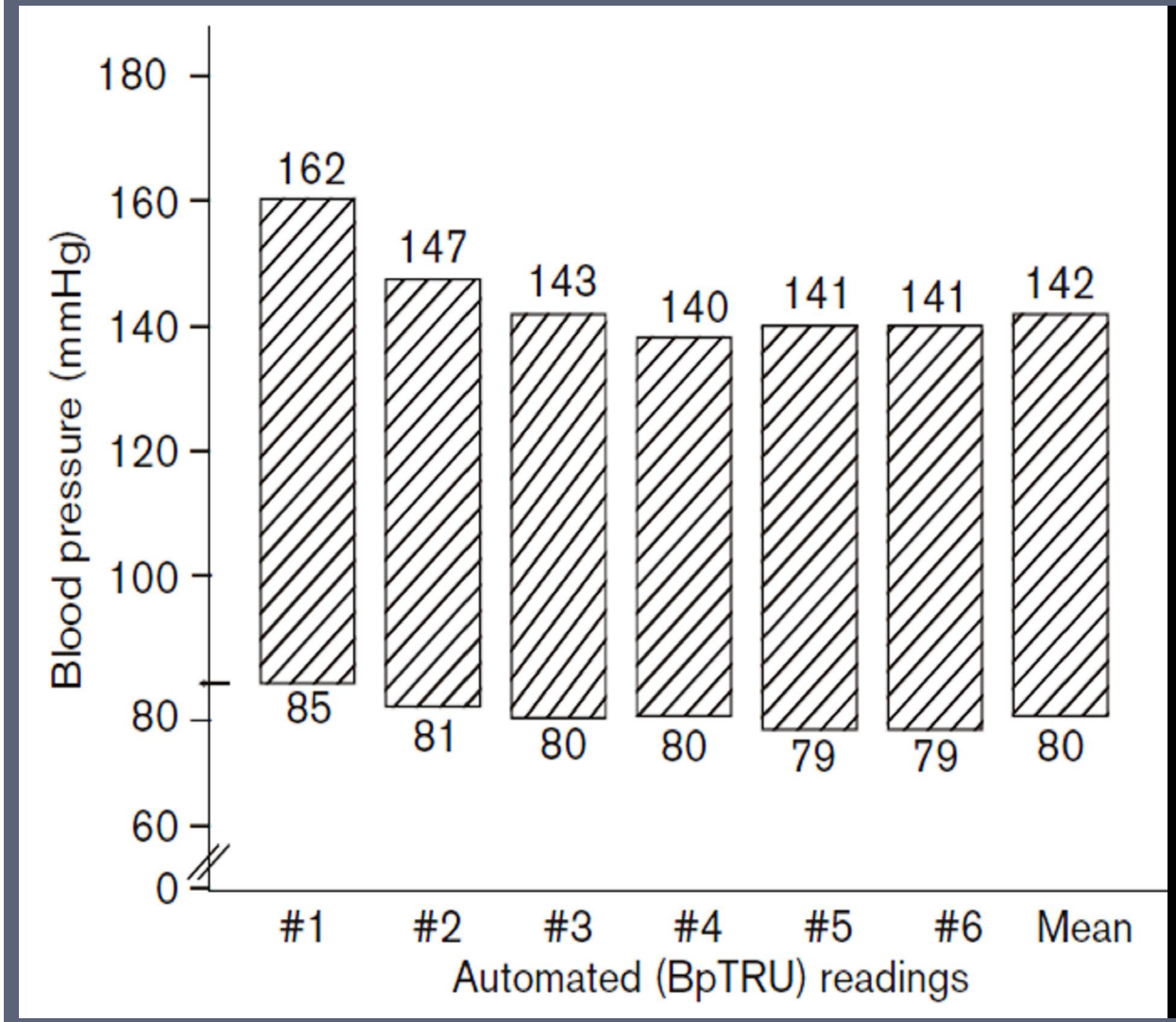
Liver enzymes Nl Ca^{++} 9.2 TSH 1.4

Urine alb/creat 14 A1c 6.0%

ECG HR 72 NSR; Normal (R-wave 14 mm II)

Framingham 10-year CHD Risk: 1%

Automated BP & Office Hypertension: ACCURATE and REPRESENTATIVE BP



Myers. Blood Press Monit 2006; 11:59ï 62.

Myers, et al. J Hypertens 2009; 27:280ï 286.

Canadian Hypertension Guidelines: ACCURATE MEASUREMENT OF BP

- When used under proper conditions, automated office SBP of ≥135 or DBP ≥85 should be considered analogous to mean awake ambulatory SBP of ≥135 and DBP of ≥85, respectively (Grade D).
- Using ABPM (see Section VIII), patients can be diagnosed as hypertensive if the mean awake SBP is >135 or the DBP is >85 (Grade C).

Canadian J Cardiol. 2010;26:249–258.

Blood Pressure and Diagnosis of Hypertension

Masked hypertension

- Home BP or daytime ABPM ≥135/≥85 is hypertensive range
- Masked Htn carries a prognosis similar to comparable BP elevations in and out of the office

  Mrs. LC does have pre-hypertensive range office BP readings (HTN if Canadian 2010 guidelines). However, her prognosis, in this case, is more closely related to her masked Htn.

  Evidence suggests that masked hypertension in patients with pre-hypertensive office readings unmasks quickly with >80% developing high readings in the office within 4 years.

Canadian Hypertension Education Program 2010;
Arch Intern Med 2001;161:2205–2211; *JAMA* 2004;291:1342–1349.
Julius, et al: NEJM, 2006.

Prognostic Significance of Home BP

- Patients: 4939 treated hypertensives age 70±6 yr
- Data: Baseline office and 4-day (2 readings / day) home BP taken with Omron 705 CP
- Follow-up: mean 3.2 yrs

(O=office; H=home; (-) = normal; (+) = high).

	O-/H-	O+/H+	O-/H+	O+/H-
RR	1.00	1.96	2.06	1.18

- Home BP is more strongly related to target organ damage and CV outcomes than office BP.

Arch Intern Med 2001;161:2205–2211.
JAMA 2004;291:1342–1349.

Nutrition and Hypertension Prevention and Treatment

SALT INTAKE

- For prevention and treatment of HTN, a dietary sodium intake of:
  - 1500 mg (65 mmol) per day for adults ≤ 50 years
  - 1300 mg (57 mmol) per day if age 51 to 70 years;
  - 1200 mg (52 mmol) per day if age > 70 years

(Grade B)

Canadian J Cardiol. 2010;26:249–258.

Hypertension Update 2011. Evidence Since JNC 7 that Impacts Patient Care

A case-based approach:

- BP Measurement & Hypertension Dx
- **Initial therapy mono-Rx,** combo-Rx
- Treatment Resistant Hypertension
- Diabetic Hypertensive
- Elderly and Very Elderly Hypertensive
- Summary

Recommendations for Individuals with Diastolic ± Systolic HTN

- Initial therapy should be monotherapy with a thiazide diuretic (Grade A); a beta-blocker (in patients <60 years, Grade B); an ACEI (in nonblack patients, Grade B); a long acting CCB (Grade B) or an ARB (Grade B). If there are adverse effects, another drug from this group should be substituted.

Canadian Hypertension Guidelines 2010;
Canadian J Cardiol. 2010;26:249–258.

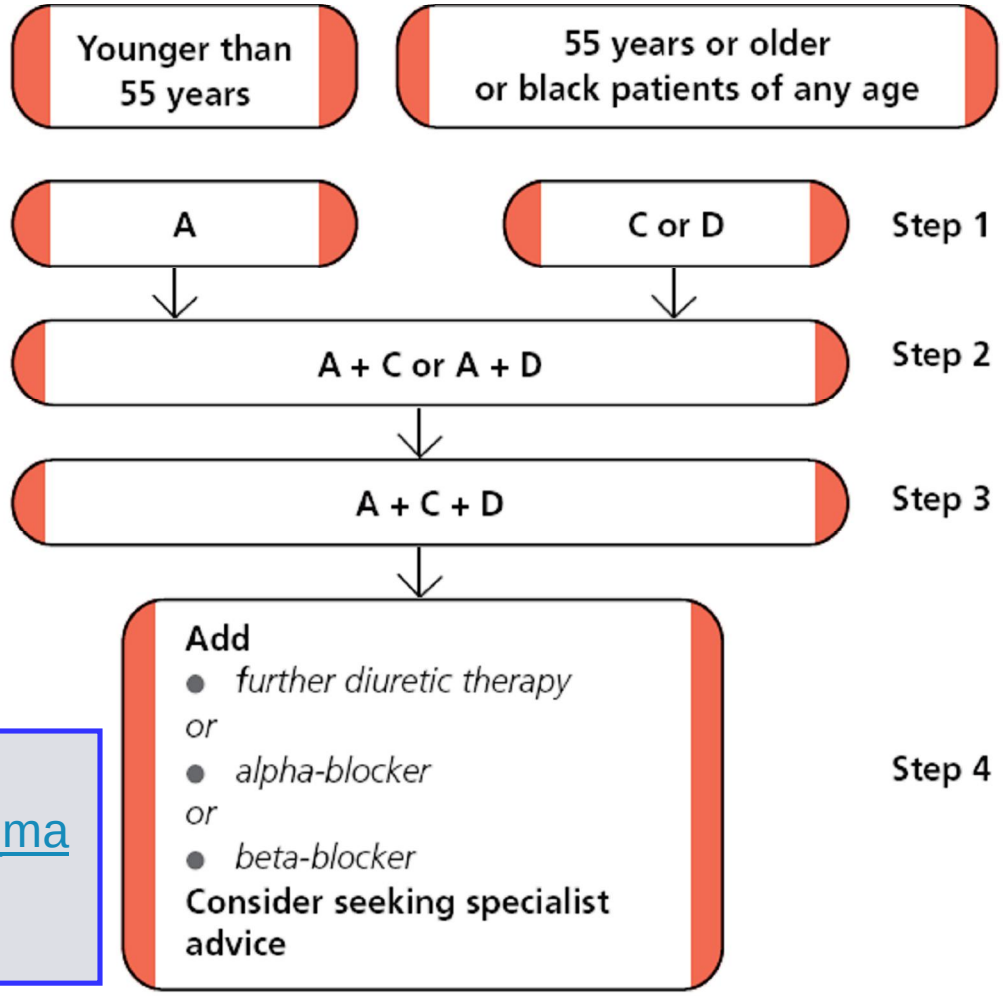
BHS

NHS
National Institute for
Health and Clinical Excellence

Choosing drugs for patients newly diagnosed with hypertension

Abbreviations:
A = ACE inhibitor
(consider angiotensin-II receptor antagonist if ACE intolerant)
C = calcium-channel blocker
D = thiazide-type diuretic

Black patients are those of African or Caribbean descent, and not mixed-race, Asian or Chinese patients



2006 Update
http://www.bhsoc.org/latest_BHS_management_guidelines.stm

Initial Pharmacotherapy of Hypertension

Mrs. LC wanted to avoid antihypertensive meds and agreed to follow the low Na^+ DASH Eating Plan and extend her walks to 30 minutes morning and evening for the next 6 months.

Mrs. LC is now 54 years old; office BP 146/86 and consistent with home readings in the past month. Her weight is 156# (BMI 25.3; WC 34.5"). Repeat labs show:

FBS 108	K+ 4.2	Creat 1.0	(eGFR 62)
TC 198	TG 150	HDL 52	LDL 116
urine alb/creat 19		A1c 6.4%	FRS 1%

Initial Pharmacotherapy of Hypertension

Which of the following is the preferred choice for initial treatment of Mrs. LC's hypertension?

1. Chlorthalidone
2. Metoprolol
3. Amlodipine
4. Lisinopril
5. Doxazosin

Initial Pharmacotherapy of Hypertension

LISINOPRIL

While thiazide diuretics were preferred as initial therapy for most patients in JNC 7, including patients with metabolic syndrome, that is likely to change in JNC 8.

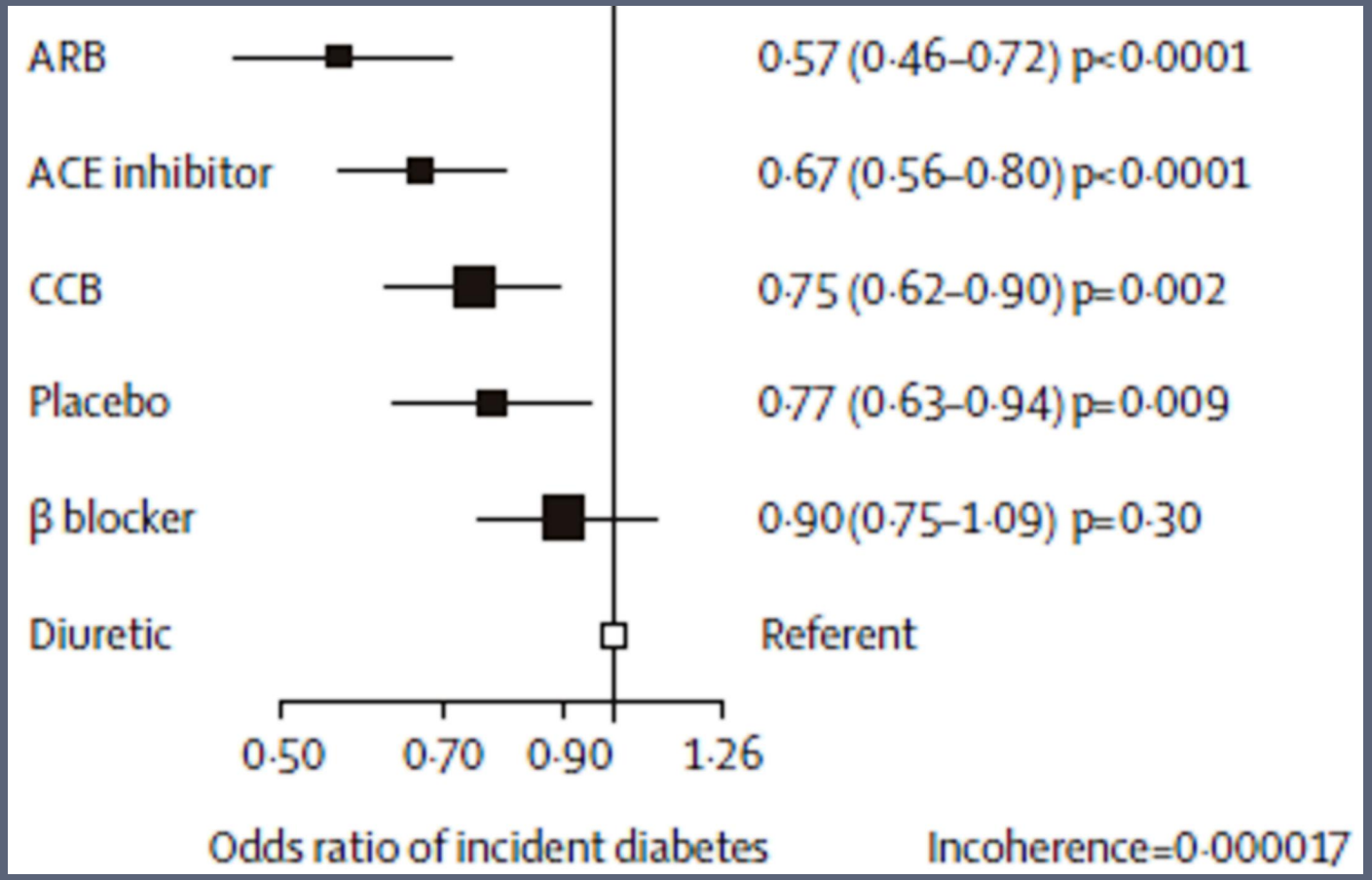
Specifically, diuretics will probably not be preferred as initial therapy in patients with the pre-diabetes and the metabolic syndrome given an excess of new onset T2D

In the absence of compelling indications, β-blockers are being viewed as 2nd and more often 3rd line choices

While CCBs are an option, evidence suggests ACEI (and ARBs) are better for preventing progression to diabetes in hypertensive patients and limiting progression to CKD

Incident Diabetes in Clinical Trials of Antihypertensive Medications

22 trials with 143,153 Pts incl 17 Htn studies



Elliott WJ, Meyer PM. Lancet 2007;369:201–207.

Hypertension Update 2011. Evidence Since JNC 7 that Impacts Patient Care

A case-based approach:

- BP Measurement & Hypertension Dx
- Initial therapy mono-Rx, **combo-Rx**
- Treatment Resistant Hypertension
- Diabetic Hypertensive
- Elderly and Very Elderly Hypertensive
- Summary

Selecting Combination Therapy

Mrs. LC has done well on Lisinopril 40 mg daily the past 2 years. BP ~126/78 at home and in office. Urine alb/creat decreased from 19 to 8. Other labs unchanged.

3 mo ago she sprained her knee and has stopped walking. She watches more TV and snacks. Weight ↑ from 149 to 158 along with home BP to 138/86 in the past month.

She returns for a scheduled visit at age 56. BP 142/86, HR 76, wt 158, BMI 25.4, WC 34". Gr 1 KW, soft S4, ∅ edema.

FBS 108, K+ 4.4, Creat 1.0 (eGFR 62), TC 198 TG 167 HDL 50 LDL 115, alb/creat 14, HbA1c 6.3%, FRS 3%

Selecting Combination Therapy

After discussion, Mrs. LC agrees to see an orthopedic surgeon who finds a torn medical meniscus. Given the elevated BP and emerging signs of target organ change, you decide to increase her antihypertensive Rx by adding:

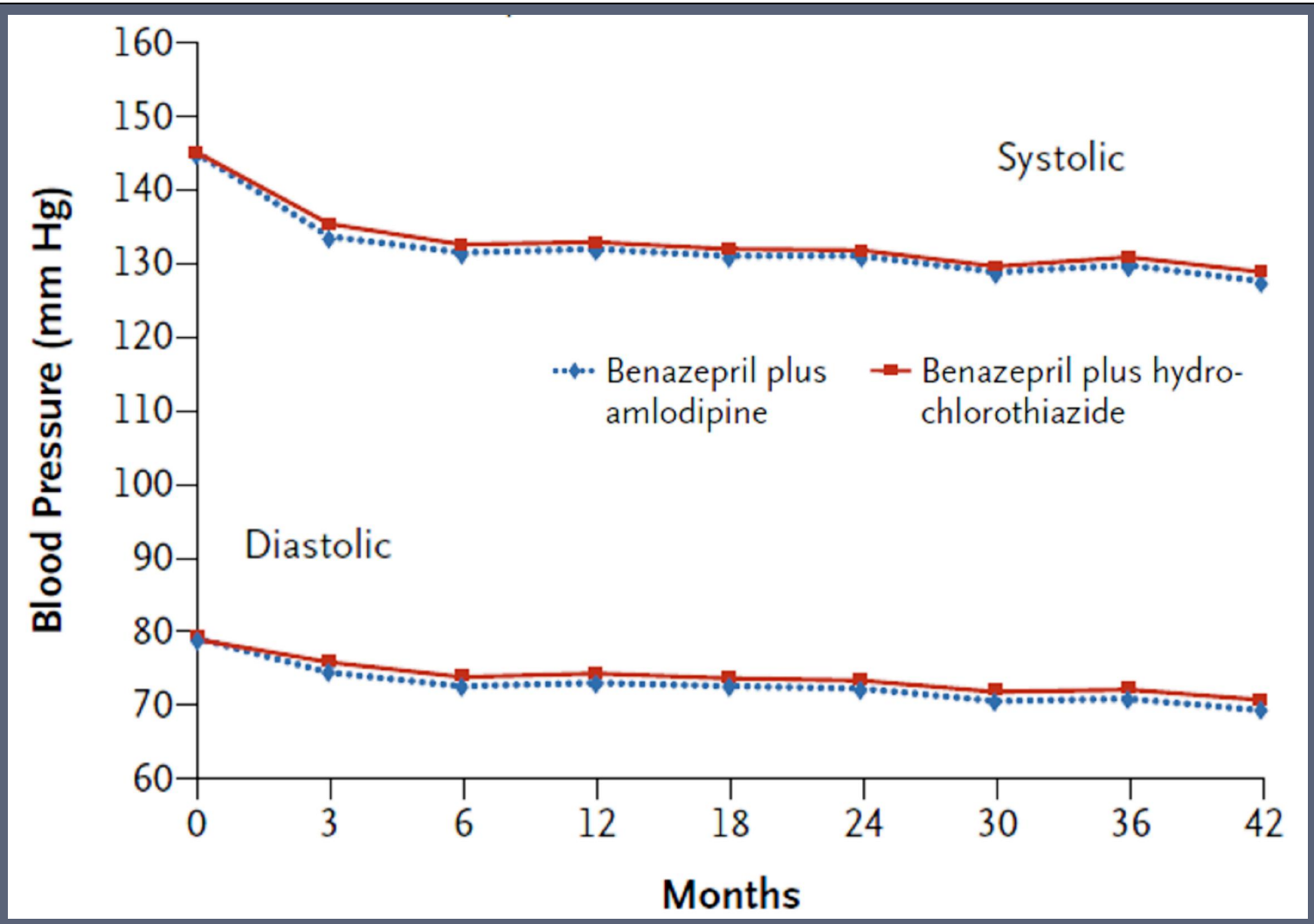
1. HCTZ 12.5 mg daily
2. Carvedilol 12.5 mg twice daily
3. Amlodipine 5 mg daily
4. Losartan 50 mg daily

Benazepril plus Amlodipine or HCTZ for Hypertension in High-Risk Patients

- *Methods* 11,506 high-risk HTN patients were randomized to benazepril+amlodipine or benazepril+HCTZ.
- *Results* BPs were 131.6/73.3 with ACEI–CCB and 132.5/74.4 with ACEI–HCTZ. There were 552 primary events with ACEI-CCB (9.6%) and 679 with ACEI–HCTZ (11.8%), HR, 0.80, p<0.001. For the secondary end point of death from CV causes, nonfatal MI, and nonfatal stroke, the HR was 0.79 (95% CI, p=0.002).
- *Conclusions* Benazepril+amlodipine was superior to benazepril+HCTZ in reducing CV events in high risk HTN

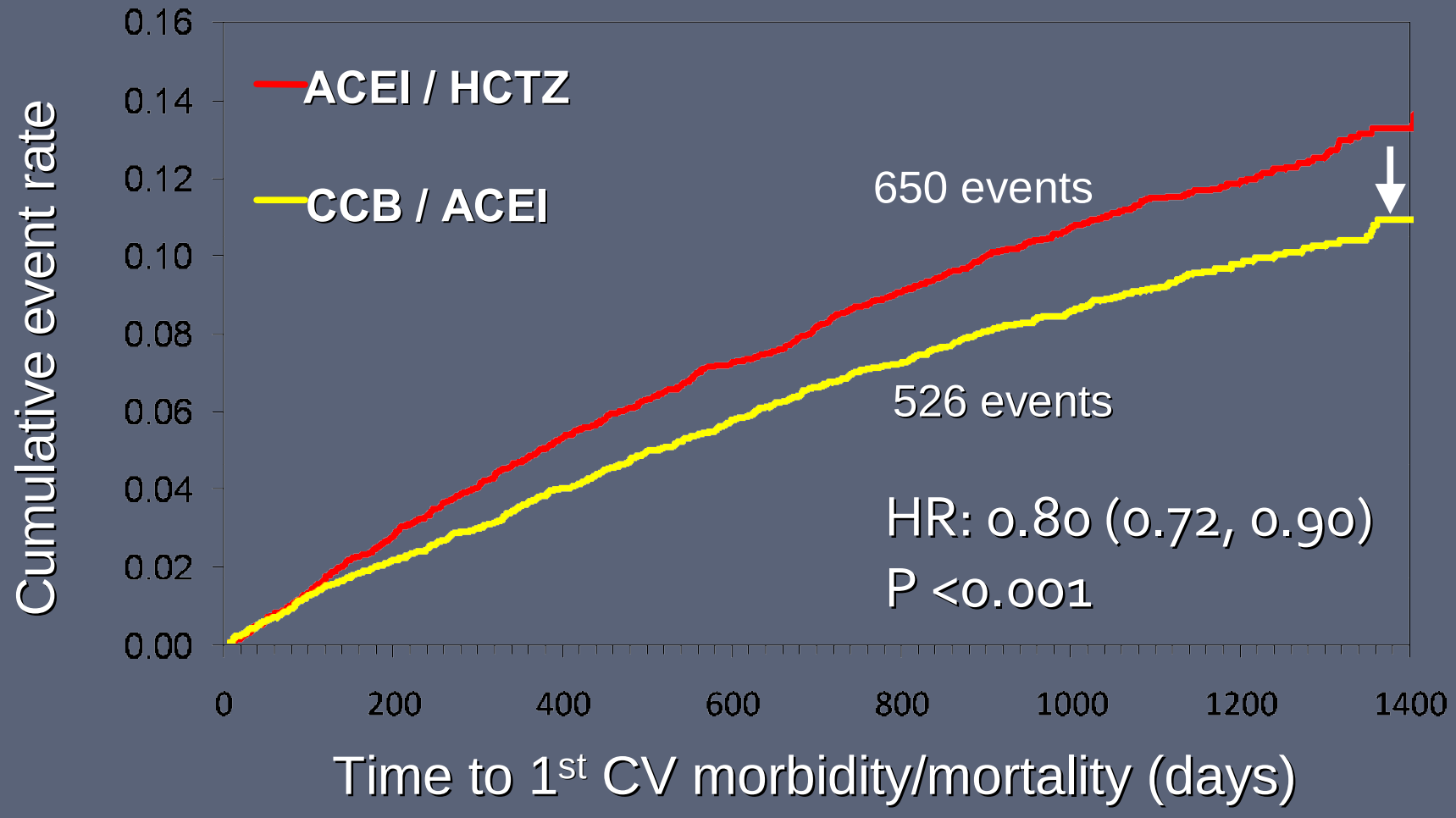
Jamerson K, et al. NEJM 2008;359:2417–2928

Blood Pressure Control in ACCOMPLISH



Jamerson K, et al. NEJM 2008;359:2417–2928

ACCOMPLISH Results:
Composite CV Morbidity and Mortality



Jamerson K, et al. NEJM 2008;359:2417–2428.

ACCOMPLISH: Outcomes in T2D

	ACEI-Amlodipine (N=5744)	ACEI-HCTZ (N=5762)	Hazard Ratio (95% CI)
Primary End Point CVE and CVD death			
Sex			
Male	10.6%	13.1%	0.80 (.69–.91)
Female	**8.1%**	**9.7%**	**0.80 (.68–1.01)**
Diabetes			
Yes	**8.8%**	**11.0%**	**0.79 (.68–.91)**
No	10.8%	13.0%	

Jamerson K, et al. NEJM 2008;359:2417ï 28.

STITCH STUDY: Main Results

Variable	Usual Care	STITCH	P-Value
# of patients	1246	802	
Baseline			
BP, mmHg	153/88	155/88	NS/NS
FDC, %	9	11	NS
Final visit			
ΔBP, mmHg	−18/8	−23/10	<.005/.05
FDC, %	15	85	<0.001
Med titration, %	70	83	<0.01
BP control, %	53	65	<0.05

Feldman RD, et al: Hypertension 2009;53:646–653.

Selecting Combination Therapy

- Benazepril/amlodipine was superior to benazepril/HCTZ in reducing CV events with similar BP control, somewhat less dizziness and hypotension but more edema
- Use of fixed-dose combinations produced better BP control in primary care than guideline-based care
- BP declines more rapidly and control rates are better with single-pill combinations than sequential Rx
- Adherence is better with fixed-dose combinations than with the same pills prescribed separately

Selecting Combination Therapy

Going forward, guidelines recommendations will likely:

- Encourage healthcare professional to more strongly consider single-pill combinations that are thiazide and CCB-based with ACEI or ARB for hypertensive patients ≥20/≥10 mmHg from goal as initial therapy and for combination therapy in patients requiring 2 meds
- Thiazide diuretics will no longer be recommended above dihydropyridine CCBs as one of the agents for patients on two antihypertensive medications

Hypertension Update 2011. Evidence Since JNC 7 that Impacts Patient Care

A case-based approach:

- BP Measurement & Hypertension Dx
- Initial therapy mono-Rx, combo-Rx
- Treatment Resistant Hypertension
- Diabetic Hypertensive
- Elderly and Very Elderly Hypertensive
- Summary

Resistant Hypertension

Definitions:

- Refractory hypertension: Mean BP ≥140/90 (above goal) on a rational 2 med regimen prescribed at optimal doses
- Resistant hypertension: Mean BP ≥140/90 (above goal) on a rational ≥3 med regimen or BP controlled on ≥4 meds preferably including a diuretic

Hypertension Can Get More Complicated

History: Mrs. LC (age 60 yrs) returns for a scheduled visit. She has done well for the past 4 years on lisinopril 40 and amlodipine 5 mg daily except for 1+ pre-tibial edema. She broke her leg and has gained 20 pounds. Her home BP readings over the past year increased steadily from ~122/78 to ~152/84. She is much less active, continues to follow her DASH-low Na^+ Eating Plan, but is snacking a bit more.

Hypertension Can Get More Complicated

Exam: BP 156/82 (avg 3) HR 74 Wt 153 BMI 24.7
Fundi: Gr I KW Neck and Lungs: Nl Heart: S4
Abd: no bruits/aneurysm Ext: pulses 2+, tr edema

Lab: Glu 110 K^+ 4.2 Creat 1.1 (eGFR 519)
Chol 208 TG 160 HDL 47 LDL 129
A1c 6.4% alb/creat 22 FRS 5%

Hypertension Can Get More Complicated

You discuss with Mrs. LC that she has Stage 3 CKD, which currently requires and may continue to trigger BP goal <130/<80. While her FRS is 5%, given the IFG and CKD her actual risk is higher

You advise her to begin simvastatin 40 mg daily (HPS).

She had already tried increasing amlodipine to 10 mg daily on her own but couldn't tolerate the edema.

She would like to avoid taking a 3rd med but doesn't think a more intensive lifestyle program is sustainable.

Hypertension Can Get More Complicated

In view of all the evidence you decide to add:

1. Add HCTZ 12.5 mg daily
2. Add Carvedilol 12.5 mg twice daily
3. Add Telmisartan 40 mg daily
4. Add Diltiazem LA 180 mg daily

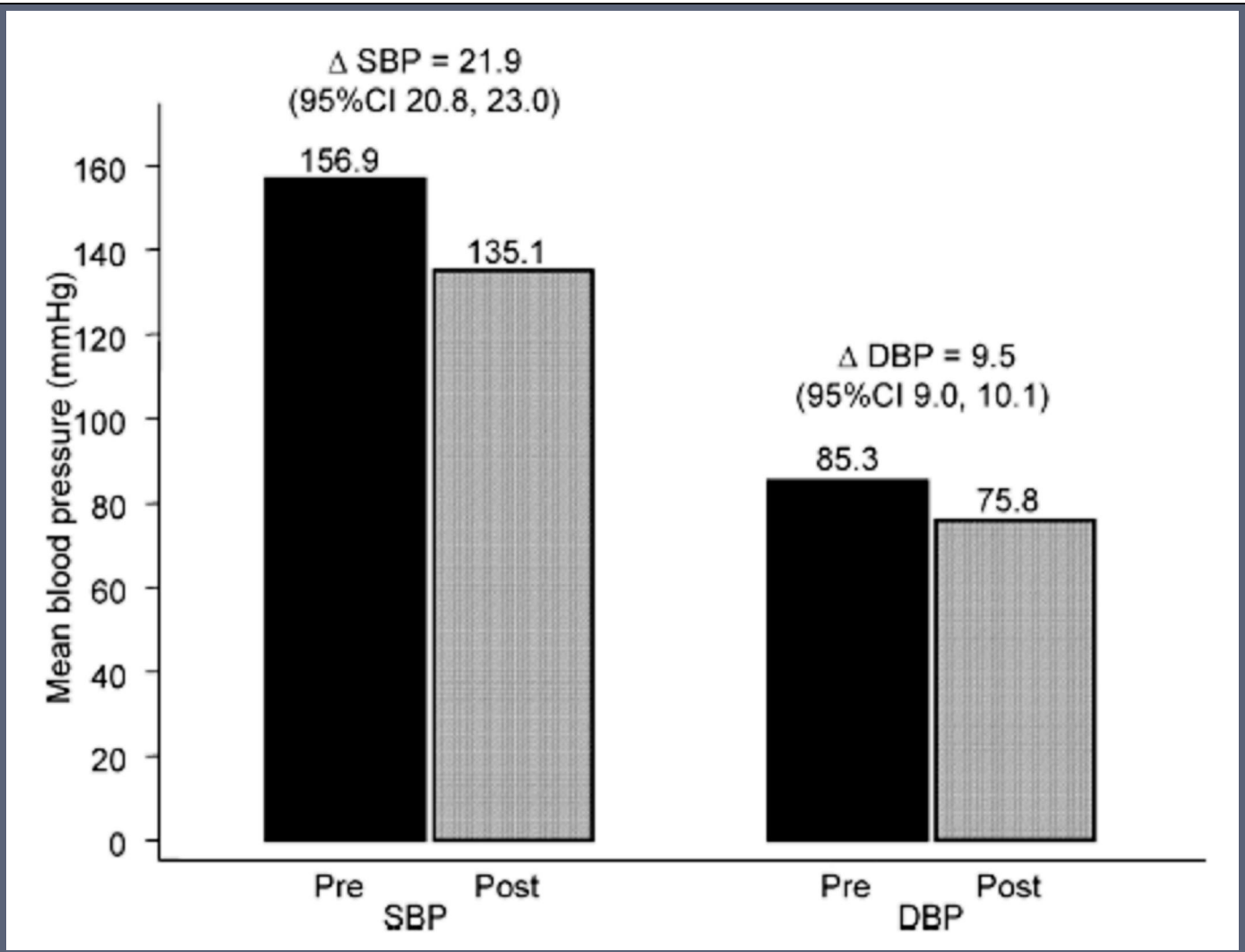
Hypertension Can Get More Complicated

She returns 1 month later and reports her home BP has fallen ~4–5 mmHg to 150/82. Repeat labs show K+ 3.6, creat 1.2, LDL 68. Office BP is 148/80.

You decide to:

1. Increase HCTZ to 25 mg daily
2. Change HCTZ to chlorthalidone 25 mg daily
3. Add Diltiazem LA 180 mg daily
4. DC HCTZ; begin HCTZ/spironolactone 12.5/12.5 /d

BP Effects of Low-Dose Spironolactone in 1411 ASCOT Hypertensives Uncontrolled on 3 Meds



Chapman, et al. *Hypertension*. 2007;49:839ï 45.

Hypertension Update 2011. Evidence Since JNC 7 that Impacts Patient Care

A case-based approach:

- BP Measurement & Hypertension Dx
- Initial therapy mono-Rx, combo-Rx
- Treatment Resistant Hypertension
- Diabetic Hypertensive
- Elderly and Very Elderly Hypertensive
- Summary

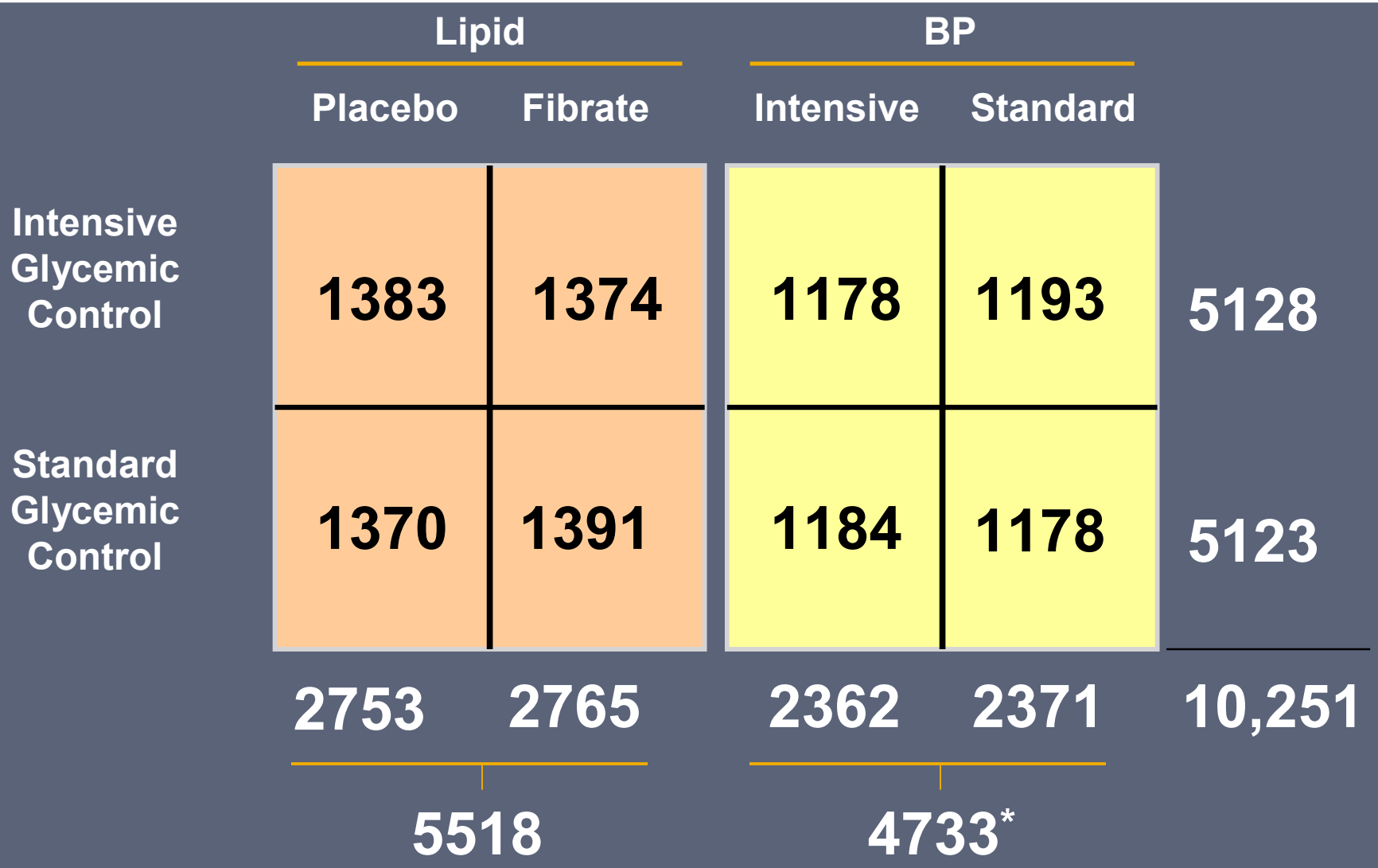
Hypertension Can Get More Complicated

Mrs. LC (age 62 yrs) returns for a scheduled visit. She has done well for the past 2 years on lisinopril 40, amlodipine 5, and HCTZ/spironolactone 12.5/12.5 daily with BP averaging 136/74.

Despite the healing of her leg fracture, she has remained sedentary and has not lost weight. She obtained labs just prior to her visit, which show FBS 128 and HbA1c 7.1%.

While not exercising, she has been surfing the web and read about the ACCORD BP Study and asks if you think her BP is okay.

ACCORD Study Design: Double 2 x 2 Factorial



N EJM 2010;362:1575-85.

* 94% power for 20% reduction in events, assuming standard group rate of 4% / yr and 5.6 yrs follow-up

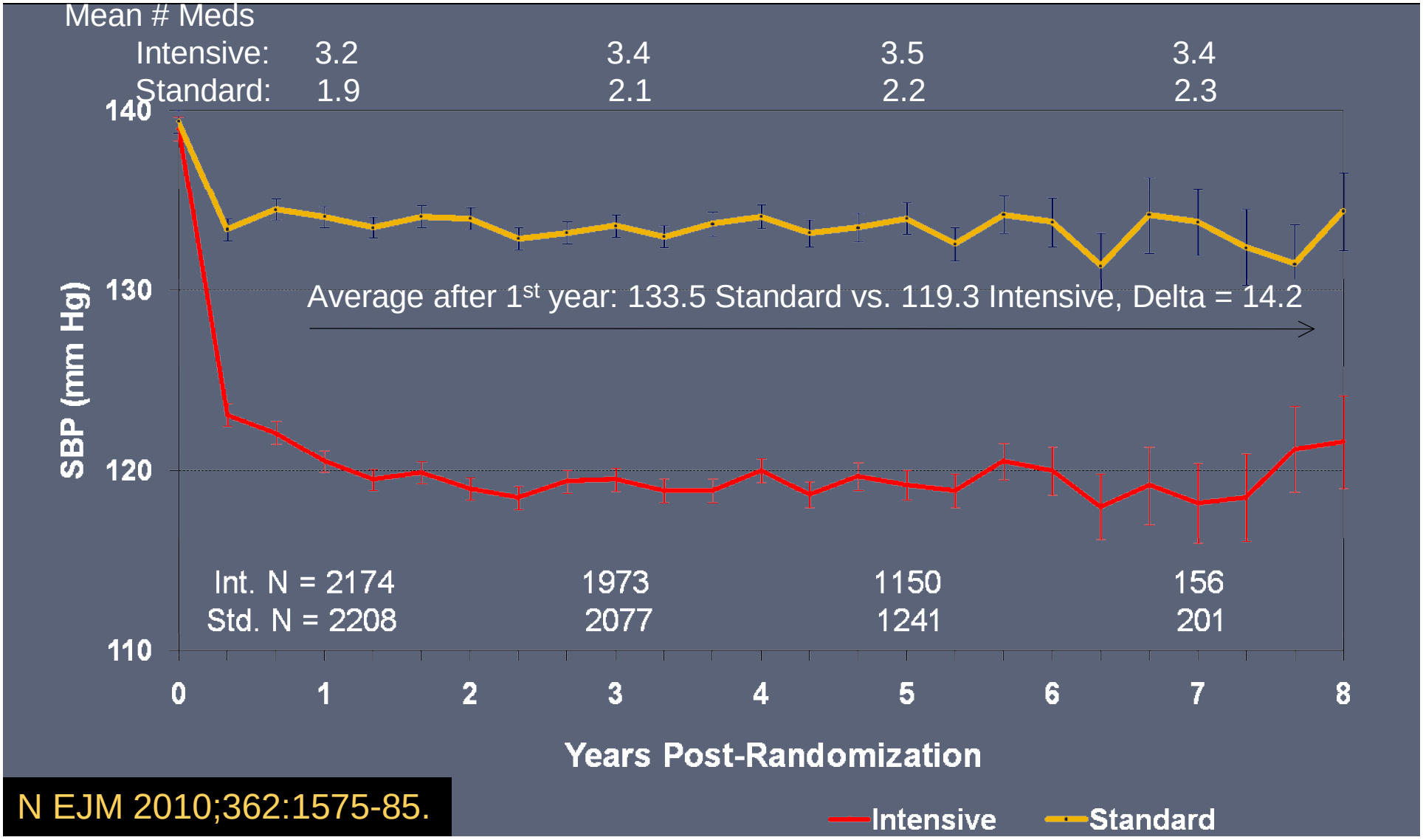
ACCORD BP Study Population: Baseline Characteristics

Characteristic	Mean or %	Characteristic	Mean or %
Age (yrs)	62	BP (mm Hg)	139/76
Women %	48	On BP meds %	87
2° prevention %	34	Creatinine (mg/dL)	0.9
Race / Ethnicity		eGFR (mL/min/1.73m^2)	92
White %	61	DM Duration (yrs)*	10
Black %	24	A1C (%)	8.3
Hispanic %	7	BMI (kg/m^2)	32

N EJM 2010;362:1575-85.

* *Median value*

ACCORD: In Study Systolic Blood Pressures



N EJM 2010;362:1575-85.

Primary & Secondary Outcomes

	<120/<80	<140/<90	HR (95% CI)	P
Primary	208 (1.87)	237 (2.09)	0.88 (0.73-1.06)	0.20
Total Mortality	150 (1.28)	144 (1.19)	1.07 (0.85-1.35)	0.55
CVD Deaths	60 (0.52)	58 (0.49)	1.06 (0.74-1.52)	0.74
Nonfatal MI	126 (1.13)	146 (1.28)	0.87 (0.68-1.10)	0.25
Nonfatal Stroke	**34 (0.30)**	**55 (0.47)**	**0.63 (0.41-0.96)**	**0.03**
Total Stroke	**36 (0.32)**	**62 (0.53)**	**0.59 (0.39-0.89)**	**0.01**

Also examined Fatal/Nonfatal HF (HR=0.94, p=0.67), a composite of fatal coronary events, nonfatal MI and unstable angina (HR=0.94, p=0.50) and a composite of the primary outcome, revascularization and unstable angina (HR=0.95, p=0.40)

N EJM 2010;362:1575-85.

ACCORD BP Study: Serious Adverse Events

Variable	Intensive Therapy (N = 2362)	Standard Therapy (N = 2371)	P Value
Serious adverse events — no. (%)†			
Event attributed to blood-pressure medications	77 (3.3)	30 (1.27)	<0.001
Hypotension	17 (0.7)	1 (0.04)	<0.001
Syncope	12 (0.5)	5 (0.21)	0.10
Bradycardia or arrhythmia	12 (0.5)	3 (0.13)	0.02
Hyperkalemia	9 (0.4)	1 (0.04)	0.01
Angioedema	6 (0.3)	4 (0.17)	0.55
Renal failure	5 (0.2)	1 (0.04)	0.12
End-stage renal disease or need for dialysis	59 (2.5)	58 (2.4)	0.93

N EJM 2010;362:1575-85.

ACCORD Conclusions

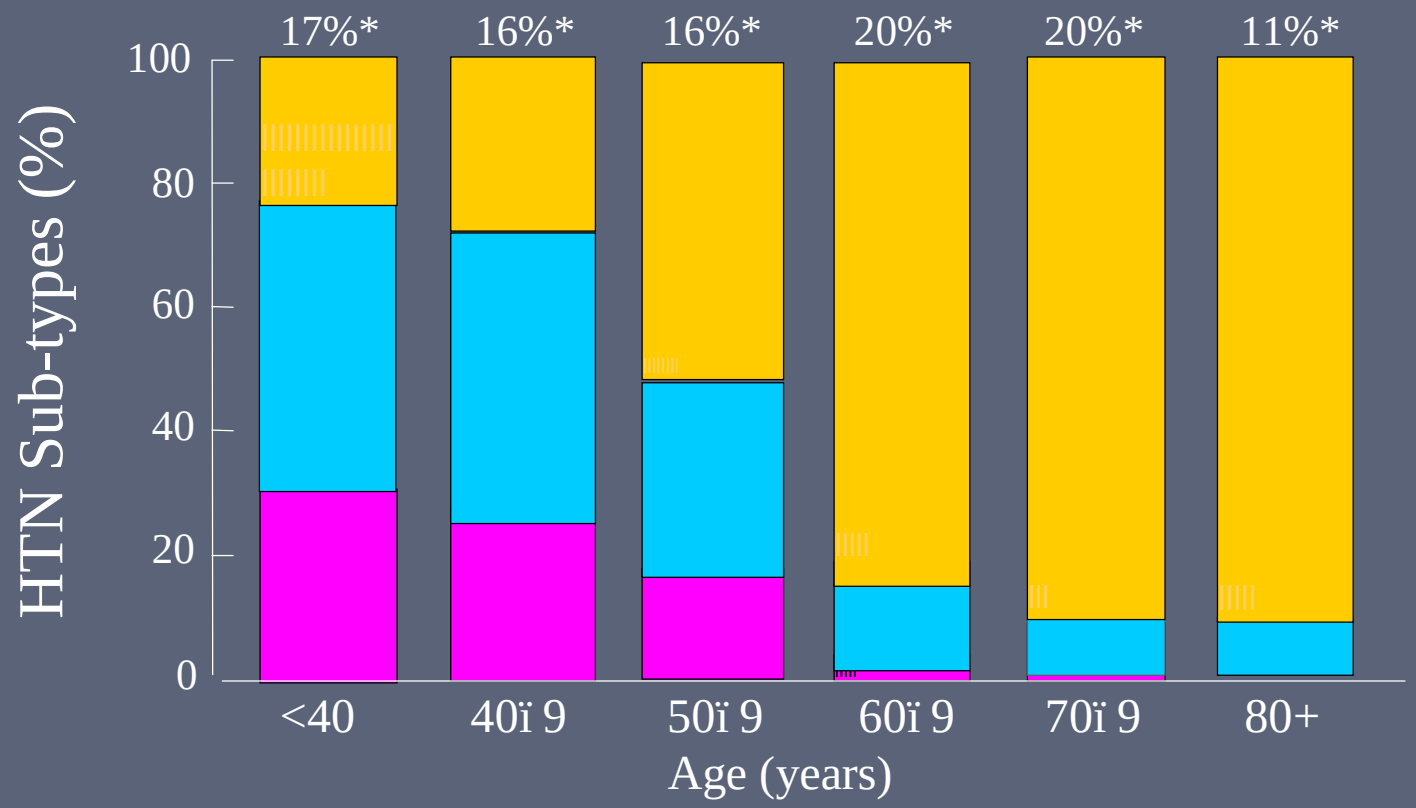
- The ACCORD BP trial evaluated the effect of targeting a SBP goal of 120 mm Hg, compared to a goal of 140 mm Hg, in patients with type 2 diabetes at increased cardiovascular risk.
- The results provide no conclusive evidence that the intensive BP control strategy reduces the rate of a composite of major CVD events in such patients.
- The reduction in stroke is consistent with meta-analyses on the impact of a 10 mm Hg reduction in SBP (relative risk=0.64) and drug treatment trials (relative risk=0.59).

Hypertension Update 2011. Evidence Since JNC 7 that Impacts Patient Care

A case-based approach:

- BP Measurement & Hypertension Dx
- Initial therapy mono-Rx, combo-Rx
- Treatment Resistant Hypertension
- Diabetic Hypertensive
- Elderly and Very Elderly Hypertensive
- Summary

Distribution of Hypertension Subtypes in *UNTREATED HYPERTENSIVES* by Age



*Numbers at top represent the overall % distribution of untreated HTN by age.

ISH (SBP ≥ 140 and DBP < 90)
SDH (SBP ≥ 140 and DBP ≥ 90)
IDH (SBP < 140 and DBP ≥ 90)

Adapted from Franklin SS et al. *Hypertension.* 2001;37(3):869ï 874.

Evidence for Treatment of Stage 2 Isolated Systolic Hypertension

Placebo-Controlled Trials

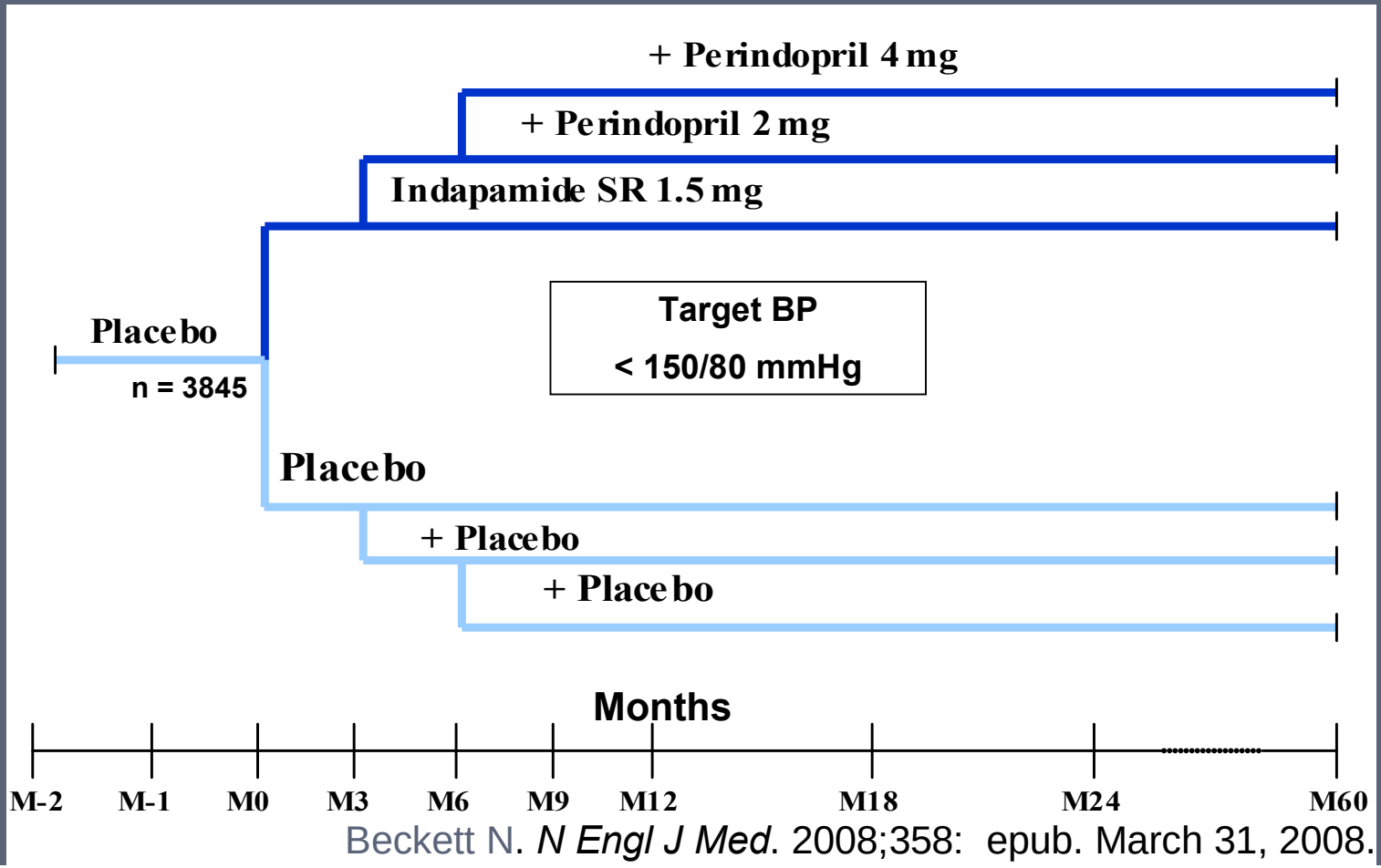
Trial	Bp_i	BP_f	ΔBP v P	ΔCVE
SHEP	170/77	143/68	12/4	0.67(0.56–0.80)
Syst-Eur	174/86	152/78	10/5	0.69(0.55–0.86)
Syst-China	170/86	150/81	8/3	0.61(0.39–0.96)
HYVET	170/91	144/80	15/6	0.66(0.53–0.82)

Active Comparator Trials

STOP-2	195/89	164/78	Non-Sig	25% less stroke with newer drugs
LIFE	174/83	156/74	Same	0.75(0.56–1.01)

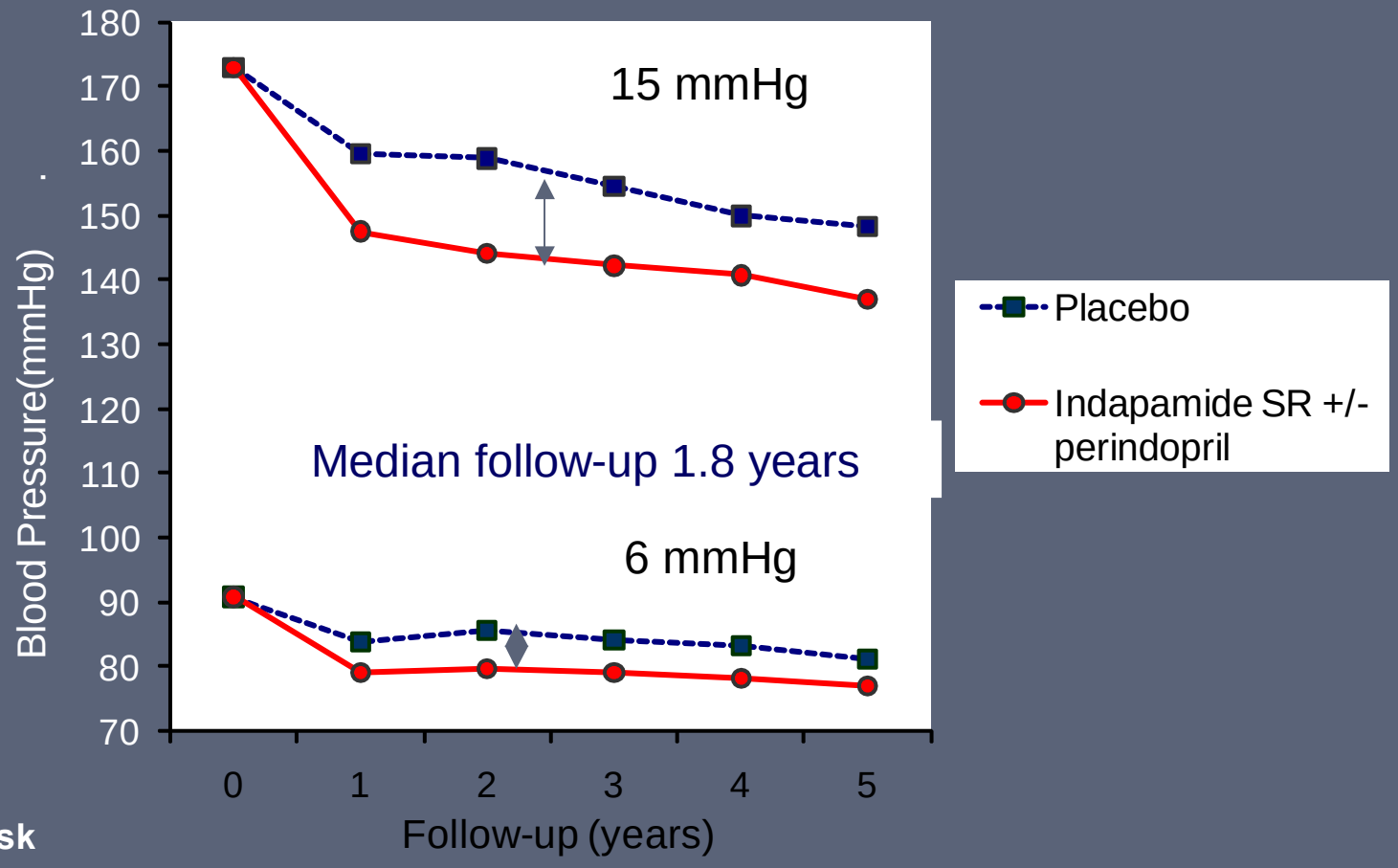
HYVET: Objectives & Design

Objective: Investigate prevention of fatal & nonfatal strokes in pts ≥80 yrs
Design: Int'l, multi-center, randomized double-blind placebo controlled
Inclusion: Age ≥ 80, SBP 160–199 + DBP <110 & informed consent



Beckett N. *N Engl J Med*. 2008;358: epub. March 31, 2008.

HYVET: Results



No. at Risk						
Placebo	1912	1468	701	330	191	116
Ind/Per	1933	1540	754	373	207	118

Beckett N. *N Engl J Med.* 2008;358: epub. March 31, 2008.

HYVET: Results.

	HR	95% CI	P value
All stroke	- 34%	0.46 - 0.95	0.025
Total mortality	- 28%	0.59 - 0.88	0.001
Fatal stroke	- 45%	0.33 - 0.93	0.021
Cardiovascular mortality	- 27%	0.55-0.97	0.029
Heart failure	- 72%	0.17-0.48	<0.001
Cardiovascular events	- 37%	0.51-0.71	<0.001

Per Protocol

Beckett N. *N Engl J Med*. 2008;358: epub. March 31, 2008.

Hypertension in the Elderly with ISH

Recommendations:

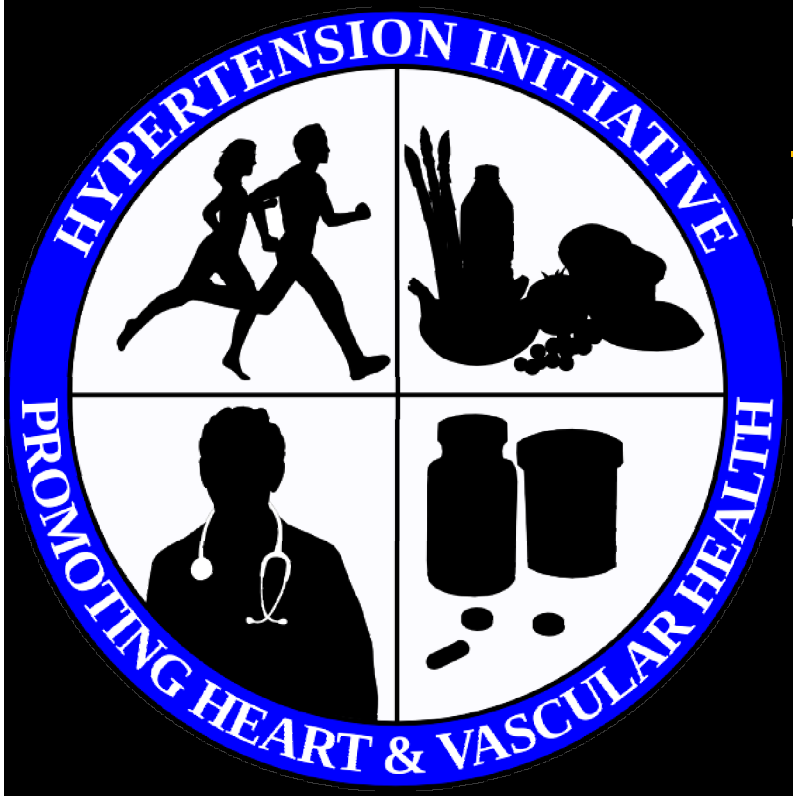
- Aim for SBP <140 in most patients to reduce CHF and stroke, but not at expense of orthostasis Sx & preferably with DBP ≥60 to minimize J-curve effect on CHD.
- Rx patients 80 and older similar to younger patients as CVD and especially CHF benefits appear to be retained. The same caveats about adverse effects and low DBP apply.

Hypertension Update 2011. Evidence Since JNC 7 that Impacts Patient Care

A case-based approach:

- BP Measurement & Hypertension Dx
- Initial therapy mono-Rx, combo-Rx
- Treatment Resistant Hypertension
- Diabetic Hypertensive
- Elderly and Very Elderly Hypertensive
- Summary

The O'QUIN Hypertension Initiative



Mission Statement:

To facilitate the transition of the Southeast from a leader in CVD to a model of heart & vascular health

Goals:

1. Improve overall health
2. Cut heart attack & stroke in ½

Strategies:

1. Healthy lifestyles – physical activity & good nutrition
2. Effective health care – access to care & medications

O'QUIN Hypertension Initiative: Opportunities

Database:

- Guide CME
- Inform practice-based CER interventions
- Preliminary data for grant applications; T2 and T3 research
- Publications: CVD and non-CVD

Network:

- Quality improvement
  —CV, diabetes
  —most chronic diseases
  —NCQA, PQRI in 2010
- CME
- Clinical Trials: T2 and T3 research incl genetic epi, pharmacogenomics

Becoming a Participant in O'QUIN & the Hypertension Initiative

- Initial contact: Talk with me (BE) directly, e-mail eganbm@musc.edu or phone (792-1715)
- Sign a Business Associate Agreement (BAA)
- Arrange for transfer of EMRS data
- Receive reports, assistance with meaningful use and QI, newsletter with free CME, opportunities for practical clinical trials / CER